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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/527,975

03/15/2005

Helene Le Buanec

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EXAMINER

WOODWARD, CHERIE MICHELLE

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

06/23/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/527,975	Applicant(s) LE BUANNEC ET AL.	
	Examiner CHERIE M. WOODWARD	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/31/2008 and 3/28/2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 11-28 is/are pending in the application.
- 4a) Of the above claim(s) 11-20 and 26-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 21-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Formal Matters

1. Applicant's Petition to Revive has been GRANTED. Applicants Response and Amendments filed 1/31/2008 are acknowledged and ENTERED. Claims 4-10 and 29 have been cancelled by Applicant. Claims 1-3, 11-28 are pending. Claims 11-20, and 26-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected inventions, there being no allowable generic or linking claim. Claims 1-3 and 21-25 are under examination. Applicant is reminded to update the status identifiers of the claims to reflect the withdrawn status of claims 26-28 in subsequent filings.

Response to Arguments

Objections/Rejections Withdrawn

2. The objection to the use of trademarks in the specification is withdrawn in light of Applicant's amendment to the specification. Applicant is cautioned NOT to include "clean" or unmarked copies of amendments in the future, as it is important that any changes to any claims, the specification, or any other part of the application be readily discernable. The multiple copies of "marked-up" and "clean" documents only serve to clutter the application file.

3. Objections and/or Rejections drawn to cancelled claims 4-10 and 29, are withdrawn as moot in light of Applicant's cancellation of these claims

4. The provisional Obviousness-Type Double Patenting Rejection over copending Application 11/135,660 is withdrawn as moot in light of the abandonment of the copending application. However, new provisional Obviousness-Type Double Patenting Rejections appear below, the rejections being necessitated by amendment. Applicant's Response on page 7 of the Remarks filed 1/31/2008 (entered by the granting of the petition to revive), states that Applicant will defer a response to the pending ODP rejection until it is no longer provisional. Applicant may not "defer" a response to a rejection. See 37 CFR 1.111(b) and MPEP 714.02. However, because the copending '660 application is abandoned, the issue is moot.

5. The rejection of claims 1-3 and 21-25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention regarding the term "less than 40% of the antigenic proteins," is withdrawn in light of Applicant's amendments to the claims.

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6. The rejection of claims 1-3 and 21-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn in light of Applicant's amendments to the claims.

7. The rejection of claims 1-3 and 21-25 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in light of Applicant's amendments to the claims.

8. The rejection of claims 1-3 and 21-24 under 35 U.S.C. 102(b) as being anticipated by Wedlock et al., (Immunol and Cell Biology. 1999; 77:28-33), are withdrawn for the reasons of record and the reasons set forth herein.

Objections/Rejections Maintained

Claim Rejections - 35 USC § 112, Second Paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claim 25 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 25 recites an immunogenic composition or a vaccine product characterized in that it comprises the CpG immunity adjuvant. The phrase "CpG immunity adjuvant" is not disclosed or otherwise defined in the specification such. The term, as recited, is confusing, is not defined in the specification, and is not commonly used in the art.

Applicant argues that "CpG immunity adjuvant" is a term that is well known in the art (Remarks, p. 10, second paragraph). In support of this argument, Applicant submits 11 abstracts of scientific articles, as Exhibit E, disclosing the use of CpG adjuvants to trigger an immune response in humans. Applicant's arguments have been fully considered, but they are not persuasive.

Claim 25, as written, recites "the CpG immunity adjuvant." [Emphasis added.] It is unclear from the claims, as written, whether Applicant is referring to the KLH of claim 1 as "the" CpG immunity adjuvant in claim 25 or whether applicant is referring to some other "CpG immunity adjuvant" as "the" CpG immunity adjuvant. Applicant's Exhibit references are noted, but they have no bearing on the instant rejection. Clarification is requested.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-3 and 21-25 remain rejected under 35 U.S.C. 102(b) as being anticipated by Zagury et al., (WO 02/011759 A1, published 2 February 2002, in French. The certified English translation of which found in US 2004/0028647 A1, the US patent application filing under 35 USC 371 PCT/FR01/02575), for the reasons of record and the reasons set forth herein.

Applicant argues that WO 02/011759 does not disclose any protein conjugate between TNF α and KLH (Remarks, p. 11, last paragraph). Applicant states that WO 02/011759 does disclose other antigenic-protein-KLH conjugates, but that the conjugates are exclusively linked by covalent bonding (Remarks, p. 11, last paragraph to page 12, last paragraph). Applicant argues that WO 02/011759 does

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not anticipate the present claims, which recite that less than 40% of the TNF α proteins are covalently linked to the KLH carrier protein (Remarks, p. 12, last paragraph).

Applicant's arguments have been fully considered, but are not persuasive. The English language translation of WO 02/0117859 (as US 2004/0028647) teaches a preferred embodiment at paragraph 50 reciting TNF α as a preferred immunogen. Contrary to Applicant's arguments, conjugation of the immunogen to KLH to a bifunctional coupling reagent is taught in a preferred embodiment at paragraph 59. Glutaraldehyde is taught as the preferred bifunctional coupling reagent in an anti-TNF α vaccine conjugate is taught at paragraph 134 (Preparation 6). These specific citations were expressly recited in the Office Action of 1/23/2007 at page 14, second paragraph. Applicant's Exhibit references are noted, but they are not persuasive in light of the teachings of WO 02/011759.

In response to Applicant's argument that WO 02/011759 does not anticipate the present claims, which recite that less than 40% of the TNF α proteins are covalently linked to the KLH carrier protein (Remarks, p. 12, last paragraph), this assertion is testable. Absent evidence to the contrary, the TNF α -KLH conjugates taught by WO 02/0117859 inherently comprise more than 1% and less than 40% of TNF α proteins are covalently linked to the KLH carrier protein. Because the Patent Office does not have the facilities to determine whether the TNF α -KLH conjugates taught by WO 02/0117859 inherently comprise more than 1% and less than 40% of TNF α proteins are covalently linked to the KLH carrier protein, the burden is on the application to show a novel and unobvious difference between the claimed scaffold and that of the prior art. See *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (CCPA 1972) (holding at 1041, "[a]s a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith") and *Ex parte Gray*, 10 USPQ 2d 1922, 1924-25 (PTO Bd. Pat. App. & Int.).

Further, absent evidence to the contrary, the TNF α -KLH conjugates taught by WO 02/0117859 inherently comprise more than 1% and less than 40% of TNF α proteins are covalently linked to the KLH carrier protein. See, *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1348-49 (Fed. Cir. 1999) ("Because sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention.... An inherent structure, composition, or function is not necessarily known."); *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a

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compound “inherently” anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound “inherently results in at least trace amounts of” the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate).

Additionally, “the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.” *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that “just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.” *Id.* See also MPEP § 2112.01 with regard to inherency and product-by-process claims and MPEP § 2141.02 with regard to inherency and rejections under 35 U.S.C. 103. The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102. “The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness.” *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983).

Absent evidence to the contrary, WO 02/0117859 meets all of the limitations of the instant claims.

New Claim Rejections – Necessitated by Amendment
Provisional Obvious-Type Double Patenting Rejection

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d

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887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claim 1-3 and 21-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25-27 of copending Application No. 11/915,044. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 25-27 of the copending '044 application recite an immunogenic product comprising antigenic heterocomplexes of TNF α and a carrier protein and a vaccine composition comprising a stable immunogenic product comprising antigenic heterocomplexes of TNF α and a carrier protein and a pharmaceutically acceptable carrier. Conjugation of TNF α to KLH as the carrier protein is taught at page 1 of the '759 specification as a preferred embodiment (see also, page 3, lines 24-31). Use of glutaraldehyde as the bifunctional bond chemical is taught at page 8, lines 20-23). Carrier molecules where less than 40% of the TNF α molecules are bound to the carrier molecules by covalent chemical bonds is taught at page 3, lines 29-30).

Applicant is reminded that MPEP § 804 (II) states, "When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). This does not mean that one is precluded from all use of the patent disclosure." (Emphasis added). "Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)." [Emphasis added.]

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 1-3 and 21-25 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-4, 6-8, 10-12, 14-17, and 19 of copending Application No. 11/735,319. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

16. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-19 of the copending '044 application recite a pharmaceutical composition comprising TNF α conjugated to KLH as the carrier protein using glutaraldehyde as the preferred bifunctional bond chemical. immunogenic product comprising antigenic heterocomplexes of TNF α and a carrier protein and a vaccine composition comprising a stable immunogenic product comprising antigenic heterocomplexes of TNF α and a carrier protein and a pharmaceutically acceptable carrier.

The '319 application does not specifically recite that less than 40% of the TNF α proteins are covalently linked to the KLH carrier protein (Remarks, p. 12, last paragraph). However, this assertion is testable. Absent evidence to the contrary, the TNF α -KLH conjugates taught by the '319 application inherently comprise more than 1% and less than 40% of TNF α proteins are covalently linked to the KLH carrier protein. Because the Patent Office does not have the facilities to determine whether the TNF α -KLH conjugates taught by WO 02/0117859 inherently comprise more than 1% and less than 40% of TNF α proteins are covalently linked to the KLH carrier protein, the burden is on the application to show a novel and unobvious difference between the claimed scaffold and that of the prior art. See *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (CCPA 1972) (holding at 1041, "[a]s a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith") and *Ex parte Gray*, 10 USPQ 2d 1922, 1924-25 (PTO Bd. Pat. App. & Int.).

Absent evidence to the contrary, the TNF α -KLH conjugates taught by the '319 application inherently comprise more than 1% and less than 40% of TNF α proteins are covalently linked to the KLH carrier protein. See, *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1348-49 (Fed. Cir. 1999) ("Because sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention.... An inherent structure, composition, or function is

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not necessarily known.”); *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a compound “inherently” anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound “inherently results in at least trace amounts of” the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

NO CLAIM IS ALLOWED.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:00am-5:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CMW/

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/Gary B. Nickol /

Supervisory Patent Examiner, Art Unit 1646